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HUMAN *XRCC2* DNA REPAIR GENE IS HOMOLOGOUS TO YEAST *RAD51*; N. Liu, J.E. Lamerdin*, L.S. Narayana*¶, M.J. Siciliano*¶, A.V. Carrano*, Z.-Q. Zhou*# , C.A. Walter*#, and L.H. Thompson, Lawrence Livermore National Lab., Livermore, CA, 94550, ¶Univ. of Texas M.D. Anderson Cancer Center, Houston, TX 77030, #Univ. of Texas Health Science Center at San Antonio, San Antonio, TX 78284

The hamster V79 cell mutant irs1 is hypersensitive to a broad variety of DNA damage, especially DNA cross-linking caused by mitomycin C (MMC). The human gene that corrects irs1 was named *XRCC2* (1). To isolate the gene, an EBV-derived cDNA expression library (kindly supplied by Dr. Legerski), was transfected into irs1 cells. Two transformants (I-PT4 and I-PT5) were obtained after selection with MMC and hygromycin B. Both clones were ~10-fold more resistant to MMC than irs1 cells. They were also partially corrected for sensitivity to cisplatin and ethyl methanesulfonate. An episomal plasmid (pEBS-XR2) with a cDNA insert of ~3 kb was recovered from the Hirt extract of I-PT5. The cDNA insert was mapped to 7q36 by Southern blotting of a hybrid clone panel, which agrees with the localization of the gene using somatic cell hybrids (1). The open reading frame (ORF) in pEBS-XR2 consists of 840 bp, encoding 280 amino acids. In addition to the original cDNA clone pEBS-XR2, we isolated 4 other cDNAs of different sizes by PCR from Legerski's pEBS7 libraries and sequenced them. All of the cDNAs contain the same ORF as identified in pEBS-XR2. Thus the ORF in pEBS-XR2 appears to be complete. The predicted protein sequence shows weak similarity with *S. cerevisiae* RAD51 (a recombinational repair protein) and its highly conserved human homolog (HHR51). XRCC2 protein is also homologous to XRCC3, another RAD51 homolog obtained by functional correction of hypersensitivity to MMC in the mutant CHO irs1SF (2). Northern hybridization gave a single transcript of 1.8 kb in baboon tissue, and the level of *XRCC2* gene expression is markedly higher in testis than in other tissues in baboon. Thus, the homology with RAD51 and the high testis expression suggest a role for XRCC2 in a DNA recombinational pathway that efficiently repairs DNA cross-links. (Work was done under the auspices of the U.S. DOE by LLNL under contract No. W-7405-ENG-48.

1. Jones et al, Genomics 26, 619-622, 1995
2. Tebbs et al, PNAS U.S.A. 92, 6354-6358, 1995